

## CURRICULUM VITAE

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 Date of birth: June 3, 1959  
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### Education

B.S. degree, Biochemistry, University of California, Davis, June 1981  
 Ph.D. degree, Biochemistry, University of Washington, March 1987  
 M.D. degree, University of Washington, June 1988  
 Postdoctoral Fellow, Genetics, Harvard Medical School, July 1988-April 1992

### Scholarships and Awards

American Heart Association Established Investigator Award  
 Arnold and Mabel Beckman Young Investigators Award  
 Lucille Markey Award  
 Medical Scientist Training Program  
 American Heart Association Student Research Associates Program

### Positions Held

10/1/04-present Interim Head, Department of Molecular Biology and Pharmacology  
 4/02-present Alumni Endowed Professor of Molecular Biology and Pharmacology  
 7/00-present Professor, Department of Molecular Biology and Pharmacology, Washington University Medical School.  
 11/96-6/00. Associate Professor, Department of Molecular Biology and Pharmacology, Washington University Medical School.  
 5/92-10/96. Assistant Professor, Department of Molecular Biology and Pharmacology, Washington University Medical School.  
 7/88-4/92. Postdoctoral Fellow with Dr. Philip Leder, Department of Genetics, Harvard Medical School. Development of a yeast GAL4/UAS binary genetic system to regulate transgene expression in mice. Expression of the *int2* gene in the mammary gland and prostate of transgenic mice. Biochemical analysis of FGF2/FGF receptor binding interactions. Cloning of a novel FGF receptor. Deregulated expression of Leukemia inhibitory factor in T-cells of transgenic mice. Transactivation of HTLV-I LTR-*myc* fusion genes by the HTLV-I-*tax* gene in transgenic mice.  
 7/83-3/87. Ph.D. thesis research with Dr. Richard Palmiter, Department of Biochemistry, University of Washington. Regulation of tissue-specific gene expression in the pancreas and liver of transgenic mice. Targeted oncogenesis of the mouse pancreas with SV40 T antigen and H-*ras*.  
 1/80-6/81. Undergraduate research with Dr. Irwin H. Segel, Department of Biochemistry, University of California, Davis. The kinetic mechanism of the enzyme Nitrate Reductase.  
 1/79-12/79. Undergraduate research with Dr. Don Bergstrom, Department of Chemistry, University of California, Davis. Synthetic organic chemistry of nucleosides.

1/77-8/79. American Heart Association Student Research Associates Program with Dr. George Popjak, Department of Biological Chemistry, University of California, Los Angeles. Enzymology of cholesterol biosynthesis.

### **Patents**

Yayon, A., Ornitz, D.M., Klagsbrun, M., Leder, P. (1993) Cells expressing a substantial number of surface high affinity HBGF receptors but relatively few low affinity HBGF binding sites and a system for assaying binding to HBGF receptor. US Patent No. 5,270,197. Harvard Medical School

Ornitz, D.M. (1998) Method for identifying molecules that regulate FGF activity. U.S. Patent No. 5,733,893 and No. 5,891,655 (divisional). Monsanto-Searle Inc.

Ward, B., Ornitz, D.M., Deines, M., Bittick, T. (pending) Tracer reagents that enhance reaction-product analysis.-Sigma Chemical Co.

Ornitz, D.M. and Colvin, J.C. (2000) Animal model with disrupted *Fgf9* gene. Monsanto-Searle Inc., Patent No. 6,136,040.

### **Independent Funding**

#### **Past**

SBIR grant with Reliable Biopharmaceuticals, 1994, Regulators of fibroblast growth factor activity, \$16,666 total costs

Arnold and Mabel Beckman Young Investigators Award, 7/1/94-6/30/96, \$100,000/year direct costs

Monsanto/Searle research award. 1/1/94-12/31/96, \$64,000/year

Monsanto/Searle research award. 1/1/97-12/31/99, \$70,000/year

Pharmacia/Monsanto research award. 6/1/01-12/31/01, \$37,000

ZymoGenetics Inc. 11/99-10/00, \$53,260 direct . *Fgf18* function in mouse development.

American Heart Association established investigator award, Regulation of cardiac and aortic arch development by fibroblast growth factors 9 and 11, 1/1/98-12/31/01, \$75,000/year direct costs

NIH grant R01 CA60673, The role of FGF receptors in cell growth and neoplasia. 4/1/94-3/30/99; \$110,387/year direct costs, Renewed as "FGFs involved in cerebellar development". 4/1/99-1/31/04; \$153,498/year direct costs.

NIH grant R01 DC04289, (PI: Yi Rao) Molecular guidance of neuronal migration. (co-PI, DMO), 8/1/00-7/31/03.

NIH grant R01 HD35692, FGF signaling in bone growth and development, 7/1/97-6/30/01, Renewed as P01 HD39952, start date 4/1/01-3/31/06, Mechanisms of Growth and Overgrowth Syndromes, \$194,168/year direct costs.

Pfizer grant, Modulation of cardiac hypertrophy by FGF signaling. 1/01/04-12/31/05, \$100,000/year direct costs

March of Dimes, Regulation of Lung Development by Fibroblast Growth Factor 9. 6/1/02-5/31/05, \$74,142/year direct costs.

#### **Current**

NIH grant RO1 DC02236, Genes involved in the development of vestibular otoconia, 1/1/95-12/31/98, Renewed, 7/1/99-6/31/04, 7/21/04-6/30/07

March of Dimes, Signaling pathways regulating lung mesenchyme development. 6/1/06-5/31/09

NIH R01 HL076664-04, FGF regulation of cardiac development and function, 12/01/04-11/30/08.

NIH R01 HD049808, FGFs in skeletal development, vasculogenesis and repair, 8/1/2006-5/31/2011.

Pending

NIH R21, Regulation of neuronal function by intracellular FGFs

NIH grant RO1 DC02236, Genes involved in the development of vestibular otoconia, renewal

Publications (Peer reviewed)

1. Renosto, F., Ornitz, D. M., Peterson, D., and Segel, I. H. (1981), Nitrate reductase from *Penicillium chrysogenum*: purification and kinetic mechanism, *J. Biol. Chem.* 256, 8616-8625
2. Ornitz, D. M., Palmiter, R. D., Hammer, R. E., Brinster, R. L., Swift, G. H., and MacDonald, R. J. (1985), Specific expression of an elastase human growth hormone fusion gene in pancreatic acinar cells of transgenic mice, *Nature* 313, 600-603
3. Ornitz, D. M., Palmiter, R. D., Messing, A., Pinkert, C. A., and Brinster, R. L. (1985), Elastase I promoter directs expression of human growth hormone and SV40 T antigen to pancreatic acinar cells in transgenic mice, *Cold Spring Harb. Symp. Quant. Biol.* 50, 399-409
4. MacDonald, R. J., Hammer, R. E., Swift, G. H., Ornitz, D. M., Davis, B. P., Palmiter, R. D., and Brinster, R. L. (1986), Tissue-specific expression of pancreatic genes in transgenic mice, *Annals of the New York Academy of Sciences* 478, 131-146
5. Hammer, R. E., Swift, G. H., Ornitz, D. M., Quaife, C. J., Palmiter, R. D., Brinster, R. L., and MacDonald, R. J. (1987), The elastase I regulatory element is an enhancer that directs correct cell-specificity and developmental onset of expression in transgenic mice, *Mol. Cell. Biol.* 7, 2956-2967
6. Ornitz, D. M., Hammer, R. E., Messing, A., Palmiter, R. D., and Brinster, R. L. (1987), Pancreatic neoplasia induced by SV40 T antigen expression in acinar cells of transgenic mice, *Science* 238, 188-193
7. Ornitz, D. M., Hammer, R. E., Palmiter, R. D., and Brinster, R. L. (1987), Promoter and enhancer elements from the rat elastase I gene function independently of other inducible and constitutive regulatory elements, *Mol. Cell. Biol.* 7, 3466-3472
8. Pinkert, C. A., Ornitz, D. M., Brinster, R. L., and Palmiter, R. D. (1987), An albumin enhancer located 10 kb upstream functions along with its promoter to direct efficient, liver-specific expression in transgenic mice, *Genes Dev.* 1, 268-276
9. Quaife, C. J., Pinkert, C. A., Ornitz, D. M., Palmiter, R. D., and Brinster, R. L. (1987), Pancreatic Neoplasia Induced by Ras Expression in Acinar Cells of Transgenic Mice, *Cell* 48, 1023-1034
10. Ornitz, D. M., Moreadith, R. W., and Leder, P. (1991), Binary system for regulating transgene expression in mice: Targeting int-2 gene expression with yeast GAL4/UAS control elements, *Proc. Natl. Acad. Sci. USA* 88, 698-702
11. Yayon, A., Klagsbrun, M., Esko, J. D., Leder, P., and Ornitz, D. M. (1991), Cell surface, heparin-like molecules are required for binding of basic fibroblast growth factor to its high affinity receptor, *Cell* 64, 841-848

12. Benvenisty, N., Ornitz, D. M., Bennett, G. L., Sahagan, B. G., Kuo, A., Cardiff, R., and Leder, P. (1992), Brain tumors and lymphomas in transgenic mice that carry HTLV-I LTR/*c-myc* and *Ig/tax* genes., ***Oncogene***. 7, 2399-2405
13. Ornitz, D. M., Cardiff, R. D., Kuo, A., and Leder, P. (1992), *Int-2*, an autocrine and/or ultra-short-range effector in transgenic mammary tissue transplants, ***J. Natl. Canc. Inst.*** 84, 887-892
14. Ornitz, D. M., and Leder, P. (1992), Ligand specificity and heparin dependence of fibroblast growth factor receptors 1 and 3, ***J. Biol. Chem.*** 267, 16305-16311
15. Ornitz, D. M., Yayon, A., Flanagan, J. G., Svahn, C. M., Levi, E., and Leder, P. (1992), Heparin is required for cell-free binding of basic fibroblast growth factor to a soluble receptor and for mitogenesis in whole cells, ***Mol. Cell. Biol.*** 12, 240-247
16. Peters, K., Ornitz, D. M., Werner, S., and Williams, L. (1993), Unique expression pattern of the FGF receptor 3 gene during mouse organogenesis, ***Dev. Biol.*** 155, 423-430
17. Tutrone, R. F., Jr., Ball, R. A., Ornitz, D. M., Leder, P., and Richie, J. P. (1993), Benign prostatic hyperplasia in a transgenic mouse: a new hormonally sensitive investigatory model, ***J Urol*** 149, 633-639.
18. Chellaiah, A. T., McEwen, D. G., Werner, S., Xu, J., and Ornitz, D. M. (1994), Fibroblast growth factor receptor (FGFR) 3. Alternative splicing in immunoglobulin-like domain III creates a receptor highly specific for acidic FGF/FGF-1, ***J. Biol. Chem.*** 269, 11620-11627
19. Deng, C. X., Wynshaw-Boris, A., Shen, M. M., Daugherty, C., Ornitz, D. M., and Leder, P. (1994), Murine FGFR-1 is required for early postimplantation growth and axial organization, ***Genes Dev.*** 8, 3045-3057
20. Shen, M. M., Skoda, R. C., Cardiff, R. D., Campos-Torres, J., Leder, P., and Ornitz, D. M. (1994), Expression of LIF in transgenic mice results in altered thymic epithelium and apparent interconversion of thymic and lymph node morphologies, ***EMBO J.*** 13, 1375-1385
21. Benvenisty, N., and Ornitz, D. M. (1995), BK1: An FGF-responsive central nervous system-derived cell line, ***Growth Factors*** 12, 49-55
22. MacArthur, C. A., Lawshé, A., Xu, J., Santos-Ocampo, S., Heikinheimo, M., Chellaiah, A. T., and Ornitz, D. M. (1995), FGF-8 isoforms activate receptor splice forms that are expressed in mesenchymal regions of mouse development, ***Development*** 121, 3603-3613
23. Mathieu, M., Chatelain, E., Ornitz, D., Bresnick, J., Mason, I., Kiefer, P., and Dickson, C. (1995), Receptor binding and mitogenic properties of mouse fibroblast growth factor 3 (FGF3); modulation of response by heparin., ***J. Biol. Chem.*** 270, 24197-24203
24. Ornitz, D. M., Herr, A. B., Nilsson, M., Westman, J., Svahn, C.-M., and Waksman, G. (1995), FGF binding and FGF receptor activation by synthetic heparan-derived Di- and Trisaccharides, ***Science*** 268, 432-436

25. Westman, J., Nilsson, M., Ornitz, D. M., and Svahn, C.-M. (1995), Synthesis and fibroblast growth factor binding of oligosaccharides related to heparin and heparan sulphate, *J. Carbohydrate Chem.* 14, 95-113
26. Colvin, J. S., Bohne, B. A., Harding, G. W., McEwen, D. G., and Ornitz, D. M. (1996), Skeletal overgrowth and deafness in mice lacking fibroblast growth factor receptor 3, *Nat. Genet.* 12, 390-397
27. Lin, H. Y., Xu, J. S., Ornitz, D. M., Halegoua, S., and Hayman, M. J. (1996), The fibroblast growth factor receptor-1 is necessary for the induction of neurite outgrowth in PC12 cells by aFGF, *J Neuroscience* 16, 4579-4587
28. Naski, M. C., Wang, Q., Xu, J., and Ornitz, D. M. (1996), Graded activation of fibroblast growth factor receptor 3 by mutations causing achondroplasia and thanatophoric dysplasia., *Nat. Genet.* 13, 233-237
29. Ornitz, D. M., Xu, J., Colvin, J. S., McEwen, D. G., MacArthur, C. A., Coulier, F., Gao, G., and Goldfarb, M. (1996), Receptor specificity of the fibroblast growth factor family, *J. Biol. Chem.* 271, 15292-15297
30. Santos-Ocampo, S., Colvin, J. S., Chellaiah, A. T., and Ornitz, D. M. (1996), Expression and biological activity of mouse fibroblast growth factor-9, *J. Biol. Chem.* 271, 1726-1731
31. Venkataraman, G., Sasisekharan, V., Herr, A. B., Ornitz, D. M., Waksman, G., Cooney, C. L., Langer, R., and Sasisekharan, R. (1996), Preferential self-association of basic fibroblast growth factor is stabilized by heparin during receptor dimerization and activation., *Proc. Natl. Acad. Sci. U.S.A.* 93, 845-850
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33. Herr, A. B., Ornitz, D. M., Sasisekharan, R., Venkataraman, G., and Waksman, G. (1997), Heparin-induced self-association of fibroblast growth factor-2. Evidence for two oligomerization processes, *J Biol Chem* 272, 16382-16389
34. McEwen, D. G., and Ornitz, D. M. (1997), Determination of fibroblast growth factor receptor expression in mouse, rat and human samples using a single primer pair, *Biotechniques* 22, 1068-1070
35. Miao, H.-Q., Ornitz, D. M., Aingorn, E., Ben-Sasson, S. A., and Vlodavsky, I. (1997), Modulation of fibroblast growth factor-2 receptor binding, dimerization, signaling, and angiogenic activity by a synthetic heparin-mimicking polyanionic compound., *J. Clin. Invest.* 99, 1565-1575
36. Osterhout, D. J., Ebner, S., Xu, J., Ornitz, D. M., Zazanis, G. A., and McKinnon, R. D. (1997), Transplanted oligodendrocyte progenitor cells expressing a dominant-negative FGF receptor transgene fail to migrate *in vivo.*, *J. Neurosci.* 17, 9122-9132

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38. Greene, J. M., Li, L. Y., Yourey, P. A., Gruber, J., Carter, K. C., Shell, B. K., Dillon, P. A., Florence, C., Duan, D. R., Blunt, A., Ornitz, D. M., Ruben, S. M., and Alderson, R. F. (1998), Identification and characterization of a novel member of the fibroblast growth factor family, *Eur. J. Neurosci.* 10, 1911-1925
39. Kato, M., Wang, H., Kainulainen, V., Fitzgerald, M. L., Ledbetter, S., Ornitz, D. M., and Bernfield, M. (1998), Physiological degradation converts the soluble syndecan-1 ectodomain from an inhibitor to a potent activator of FGF-2, *Nat. Med.* 4, 691-698
40. Lin, H.-Y., Xu, J., Ischenko, I., Ornitz, D. M., Halegoua, S., and Hayman, M. J. (1998), Identification of the cytoplasmic regions of fibroblast growth factor (FGF) receptor 1 which play important roles in the induction of neurite outgrowth in PC12 cells by FGF-1, *Mol. Cell. Biol.* 18, 3762-3770
41. McEwen, D. G., and Ornitz, D. M. (1998), Regulation of the fibroblast growth factor receptor 3 promoter and intron I enhancer by Sp1 family transcription factors, *J. Biol. Chem.* 273, 5349-5357
42. Naski, M. C., Colvin, J. S., Coffin, J. D., and Ornitz, D. M. (1998), Repression of hedgehog signaling and BMP4 expression in growth plate cartilage by fibroblast growth factor receptor 3, *Development* 125, 4977-4988
43. Ornitz, D. M., Bohne, B. A., Thalmann, I., Harding, G. W., and Thalmann, R. (1998), Otoconial agenesis in *tilted* mutant mice, *Hearing Res.* 122, 60-70
44. Wang, Y., Kowalski, P. E., Thalmann, I., Ornitz, D. M., Mager, D. L., and Thalmann, R. (1998), Otoconin-90, the mammalian otoconial matrix protein contains two domains of homology to secretory phospholipase A2, *Proc. Natl. Acad. Sci., USA* 95, 15345-15350
45. Xu, X., Weinstein, M., Li, C., Naski, M., Cohen, R. I., Ornitz, D. M., Leder, P., and Deng, C. (1998), Fibroblast growth factor receptor 2 (FGFR2)-mediated regulation loop between FGF8 and FGF10 is essential for limb induction, *Development* 125, 753-765
46. Chellaiah, A., Yuan, W., Chellaiah, M., and Ornitz, D. M. (1999), Mapping ligand binding domains in chimeric fibroblast growth factor receptor molecules. Multiple regions determine ligand binding specificity, *J. Biol. Chem.* 274, 34785-34794
47. Colvin, J. S., Feldman, B., Nadeau, J. H., Goldfarb, M., and Ornitz, D. M. (1999), Genomic organization and embryonic expression of the mouse fibroblast growth factor 9 gene, *Dev. Dyn.* 216, 72-88
48. Li, H. S., Chen, J. H., Wu, W., Fagaly, T., Zhou, L. J., Yuan, W. L., Dupuis, S., Jiang, Z. H., Nash, W., Gick, C., Ornitz, D. M., Wu, J. Y., and Rao, Y. (1999), Vertebrate slit, a secreted ligand for the transmembrane protein roundabout, is a repellent for olfactory bulb axons, *Cell* 96, 807-818

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50. Wang, Y., Thalmann, I., Thalmann, R., and Ornitz, D. M. (1999), Mapping the mouse Otoconin-90 (*Oc90*) gene to chromosome 15, *Genomics* 58, 214-215
51. Xu, J., Lawshe, A., MacArthur, C. A., and Ornitz, D. M. (1999), Genomic structure, mapping, activity and expression of fibroblast growth factor 17, *Mech. Dev.* 83, 165-178
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55. Tarantino, L. M., Feiner, L., Alireza Alavizadeh, A., T., W., Hurle, B., Ornitz, D., Rowe, L. B., Webber, A. L., Raper, J., Lengeling, A., and Bucan, M. (2000), A high-resolution radiation hybrid map of the proximal portion of mouse Chromosome 5, *Genomics* 66, 55-64
56. Wang, Q., McEwen, D. G., and Ornitz, D. M. (2000), Subcellular and developmental expression of alternatively spliced forms of fibroblast growth factor 14, *Mech. Dev.* 90, 283-287
57. Xu, J. S., Liu, Z. H., and Ornitz, D. M. (2000), Temporal and spatial gradients of Fgf8 and Fgf17 regulate proliferation and differentiation of midline cerebellar structures, *Development* 127, 1833-1843
58. Yu, K., Herr, A. B., Waksman, G., and Ornitz, D. M. (2000), Loss of fibroblast growth factor receptor 2 ligand-binding specificity in Apert syndrome, *Proc Natl Acad Sci U S A* 97, 14536-14541
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70. Oh, L. Y., Denninger, A., Colvin, J. S., Vyas, A., Tole, S., Ornitz, D. M., and Bansal, R. (2003), Fibroblast growth factor receptor 3 signaling regulates the onset of oligodendrocyte terminal differentiation, *J Neurosci* 23, 883-894
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76. Yuan, W., Rao, Y., Babiuk, R. P., Greer, J. J., Wu, J. Y., and Ornitz, D. M. (2003), A genetic model for a central (septum transversum) congenital diaphragmatic hernia in mice lacking Slit3, *Proc Natl Acad Sci U S A* 100, 5217-5222
77. Amizuka, N., Davidson, D., Liu, H., Valverde-Franco, G., Chai, S., Maeda, T., Ozawa, H., Hammond, V., Ornitz, D. M., Goltzman, D., and Henderson, J. E. (2004), Signalling by fibroblast growth factor receptor 3 and parathyroid hormone-related peptide coordinate cartilage and bone development, *Bone* 34, 13-25
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106. Wozniak, DF, Xiao, M, Xu, ., Yamada, KA, and Ornitz, DM, (2007). Impaired Spatial Learning and Defective Theta Burst Induced LTP in Mice Lacking Fibroblast Growth Factor 14. *Neurobiol Dis*, 26, 14-26.
107. Xiao, M, Xu, L, Laezza, F, Yamada, K, Feng, S, and Ornitz, DM, (2007). Impaired hippocampal synaptic transmission and plasticity in mice lacking fibroblast growth factor 14. *Mol Cell Neurosci*, 34, 366-377.
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#### **Book chapters and reviews:**

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2. Ornitz, D. M. and Waksman, G. (1997). Fibroblast growth factor receptors. Growth factors and wound healing: Basic science and potential clinical applications. New York, Springer-Verlag. Ziegler, T. R., Pierce, G. F. and Herndon, D. N., 151-174.
3. Naski, M. C. and Ornitz, D. M. (1998). FGF signaling in skeletal development. Front. Biosci. 3, D781-794.
4. Thalmann, R., Echols, R., Wang, Y., Thalmann, I. and Ornitz, D. M. (1999). Unresolved issues of biology and pathology of otoconia. in Equilibrium in research and equilibration and modern treatment. Amsterdam, Elsevier Science. Clausen, C.-F. 113-119
5. Ornitz, D. M. (2000). FGFs, heparan sulfate and FGFRs: complex interactions essential for development. Bioessays 22, 108-112
6. Ornitz, D. M. (2000). Fibroblast growth factors, chondrogenesis and related clinical disorders. Skeletal growth factors. Philadelphia, Lippincott Williams & Wilkins. Canalis, E., 197-209.
7. Ornitz, D. M. and Itoh, N. (2001). Fibroblast growth factors. Genome Biology, 3005.1-3005.12.
8. Ornitz, D. M. (2001). Regulation of chondrocyte growth and differentiation by fibroblast growth factor receptor 3. In The molecular basis of skeletogenesis, G. Cardew, and J. A. Goode, eds. (Chichester, John Wiley and Sons, Ltd.), pp. 63-80.
9. Yu, K., and Ornitz, D. M. (2001). Uncoupling FGF receptor 2 activation and ligand binding specificity: Multiple paths to Apert syndrome-like phenotypes., Proc. Natl. Acad. Sci., U S A, 98, 3641-3643.
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11. Ornitz, D.M. and Marie, P. J. (2002). FGF signaling pathways in endochondral and intramembranous bone development and human genetic disease. Genes Dev., 16, 1446-1465
12. Ornitz, D. M. (2003) Evolution of Fibroblast Growth Factors, in Encyclopedia of the Human Genome, pp. in press, Nature Publishing Group, New York
13. Itoh, N., and Ornitz, D. M. (2004), Evolution of the *Fgf* and *Fgfr* gene families, Trends Genet. 20, 563-569.

14. Ornitz, D. M. (2005). FGF signaling in the developing endochondral skeleton. *Cytokine Growth Factor Rev* 16, 205-213.
15. Ornitz, D. M., and Sannes, P. (2005) FIBROBLAST GROWTH FACTORS. In: *Encyclopedia of Respiratory Medicine*, Elsevier Ltd.
16. Hughes, I., Thalmann, I., Thalmann, R., and Ornitz, D. M. (2006),. Mixing model systems: Using zebrafish and mouse inner ear mutants and other organ systems to unravel the mystery of otoconial development. *Brain Res.*
17. Lavine, KJ, Ornitz, DM, (2007), Rebuilding the coronary vasculature: hedgehog as a new candidate for pharmacologic revascularization. *Trends Cardiovasc Med* 17, 77-83.
- 18.

### **Publications in preparation or submitted**

Hedgehog signaling to distinct cell types differentially regulates coronary artery and vein development

FGF signaling regulates mesenchymal differentiation and skeletal patterning along the limb bud proximodistal axis

FGF-Wnt signaling interactions regulate lung mesoderm development.

### **Invited Seminars**

Washington University, Dept. of Genetics, October 1992; Dupont/Meck, October, 1992; New York University, Dept. of Cell Biology, April, 1994; University of Pennsylvania, Research Center in Oral Biology, April 1994; Harvard Medical School, Dept. of Genetics, June 1994; Millenium Pharmaceuticals, June 1994; Washington University, Dept. of Hematology, October 1994; Prizm Pharmaceuticals, January 1995; Jewish Hospital, St. Louis, Dept. of Medicine, June 1995; Mount Sinai Medical Center, Brookdale Center for Molecular Biology, October 1995; Purdue University, Biochemistry and Molecular Biology Program, October 1995; University of Washington, Biochemistry, February 1996; Children's Hospital, St. Louis, Pediatric Grand Rounds, June 1996; University of Connecticut Medical School, October, 1996; Bayer Pharmaceuticals Inc., October, 1996; Human Genome Science Inc., October, 1996; Hartman Institute, University of Helsinki, Molecular/Cancer Biology Laboratory, November, 1996; Ludwig Institute for Cancer Research, Stockholm Branch, Karolinska Institute, November, 1996; McGill University Medical School, March, 1997; Lady Davis Institute for Medical Research, Montreal, March, 1997; Washington University, Dept. of Neurology, April, 1997; Sigma Chemical Co., St. Louis, March 1997; Schriners Hospital, Portland, Oregon, December, 1997; Dept. of Biol. Sciences and Technology, Tokushima University, Tokushima City, and Niigata University School of Dentistry, Niigata, Japan, February 1998; University of Colorado, Boulder, April 1998; St. Louis University, Dept. of Molecular Microbiology and Immunology, February, 1999; UC Irvine, Dept. of Developmental Biology, April, 1999; SUNY, Stony Brook, Dept. of Molecular Genetics and Microbiology, April, 1999; University of Wisconsin, Madison, Dept. of Anatomy, May, 1999; Swiss Federal Institute of Technology, Zurich, October 1999; University of Washington, Dept. of Pharmacology, October, 1999; Zymogenetics Inc., Seattle, October, 1999; King's College London, Guy's Hospital campus, November, 1999;

MD Anderson Cancer Center, Houston, TX, January, 2000; NYU Medical School, NY, February, 2000; Mount Sinai Medical School, NY, February 2000; Saint Louis University, Dept. of Biology, October, 2000; Vision Science Training Grant, University of Washington, Seattle, January, 2001; Zymogenetics Inc. January, 2001; Pharmacia Inc. Kalamazoo, June, 2001;

ImClone Inc., NYC, October, 2001; UMDNJ, Newark, October, 2001; University of Leuven Medical School, Leuven, Belgium, November, 2001; Institute Curie, Paris, France, November, 2001; Max Planck Institute for Genetics, Berlin, Germany, November, 2001; Renal Division, Washington University, November, 2001; Stowers Institute for Medical Research, February, 2002; University of Chicago, Dept. of Molecular Genetics and Cell biology, March 2002; Cardiology Division, Washington University, May 2002; Salk Institute, May, 2002; Okayama University Medical School, June, 2002; Kyoto University, July, 2002; Siteman Cancer Center Basic Science Seminar Series, September, 2002; University of Oulu, October, 2002; University of Helsinki, October, 2002; Dept. Cell Biology, Washington University, November, 2002; Cell Signaling, Duke University Medical School, November, 2002; Lineberger Comprehensive Cancer Center, UNC, February, 2003; Neuroscience Center, UNC, February, 2003; Division of Cardiology, UCSD, April, 2003; Bone conference, Washington University, April, 2003; Chiba University, Japan, June, 2003; NYU Medical School, Dept. of Pharmacology, November, 2003; Shriners Hospital, Oregon health Science University, December, 2003; National Cancer Institute, Frederick, MD, February, 2004; Children's Hospital, Boston, Dept. Orthopedic Surgery, October, 2004; UT Southwestern, Dallas, Molecular Biology seminar series, November, 2004; Oxford University, Oxford, UK, December, 2004; University of Nebraska Medical School, Omaha, January, 2005; University of Southern California, February, 2005; Endocrine Grand Rounds, Massachusetts General Hospital, Boston, March, 2005; Renal division, Washington University, April, 2005; ETH Zurich, May, 2005; Pulmonary Medicine, Washington University, November, 2005; NIDCD council, January, 2006; NHGRI, January, 2006; Molecular Biology & Pharmacology, Washington University, April, 2006; University of Cincinnati, April, 2006; Genentech Inc., April, 2006; Enobia Pharmaceuticals, Montreal, April, 2006; Medical College of Georgia, May, 2006; Eli Lilly, August, 2006; University of Iowa, Dec. 2006; Radiation Oncology, Washington University, Dec. 2006; University of Utah, February, 2007; Baylor College of Medicine, April, 2007;

### **Speaker at Conferences**

International Genetic workshop on Crouzon and other Craniofacial Disorders, Philadelphia, March 1995; Gordon Conference on Collagen, July 1995; International Symposium on Growth Factors and Wound Healing: Basic Sciences and Clinical Applications (Serono Symposium USA), Boston, September 1995; Keystone Symposium on Signal Transduction through Tyrosine Kinases, March 1996; Gordon Conference on Peptide Growth Factors, August 1996; American Society for Bone and Mineral Research, Plenary speaker, Seattle, September, 1996; 2nd GAAS meeting on Molecular Medicine: The Role of Growth Factors in Human Disease, Munich, November 1996; Gordon Conference on Bone and Teeth, July 1997; Gene function *in vivo*: The Impact of Gene Targeting, Research Workshop of the Israel Science Foundation, September, 1997; Molecular Signaling in Development, Cell Differentiation and Proliferation, Tokyo Medical and Dental University, Tokyo, February 1998; Alternative Biology of Fibroblast Growth Factors, Edinburgh, Scotland, March 1998; Gordon conference on Bioengineering and Orthopedic Science, July, 1998; The Role of Cytokines in Human disease II, Kloster Seeon, Germany, August, 1998; NIDCD workshop, Role of Transgenic and Knockout Studies in Understanding Sensory-Motor Performance in Altered Gravitational Environments, Bethesda, MD, June 1999; Gordon Conference, Development, June, 1999; German Genetic Society, Developmental Genetics, Munich, October 1999; Novartis Foundation, The Molecular Basis of Skeletogenesis, London, November, 1999; EMBO Workshop of FGF and their Receptors: Structure to Function, Ein Gedi, Israel, December 1999; American Society of Human Genetics, Philadelphia, October, 2000; Biology and Pathology of the Extracellular Matrix, Plenary speaker, St. Louis, October, 2000; Keystone Symposium on Integration of Signaling Pathways in Development, January, 2001; American Heart Association, May, 2001; Gordon conference, Tissue repair and wound healing, June, 2001; Gordon

conference, Bone and Teeth, August, 2001; MD Anderson Cancer center symposium, October, 2001; International Titisee Conference, Growth Factors in Development, Repair and Disease, Titisee, Germany, March, 2002; American Society for Endocrinology, San Francisco, June, 2002; Japanese Endocrine Society, Osaka, June, 2002; Mouse Molecular Genetics, CSHL, August, 2002; Skeletal Development, Lucca, Italy, October, 2002; Arizona Cancer Center meeting on Multiple Hereditary Exostoses, Tucson, AZ, October, 2002; Birth defects meeting, NIH, December, 2002; Biology and Pathology of Cartilage, Gordon conference, Ventura, CA, March, 2003; Experimental Biology, ASBMB, San Diego, April, 2003; American Society for Neuro Chemistry, Newport Beach, May, 2003; International Society Bone and Mineral Research/Japan Society Bone and Mineral Research, Osaka, June, 2003; Ninth Canadian Connective tissue conference, Montreal, July, 2003; FASEB meeting Tucson, Growth factor tyrosine kinases, August, 2003; ASBMR, Minneapolis, September, 2003; International meeting on Fibroblast Growth Factors, Kobe, Japan, October, 2003; Gordon conference on Craniofacial Morphogenesis and Tissue Regeneration, January, 2004; Keystone symposia, Signaling in vertebrate organogenesis, February, 2004; Experimental Biology, AAA, Washington DC, April, 2004; ARVO (Association for Research in Vision and Ophthalmology), April, 2004; Leder lab reunion symposium, June, 2004; Mouse Molecular Genetics, CSHL, September, 2004; Clive Dickson symposium, London, December, 2004; Southern Illinois University 11<sup>th</sup> Annual Molecular & Cellular Biology symposium, Keynote speaker, April, 2005; Hinterzartener Kreis for Cancer Research, Cadenabbia, Italy, May, 2005; GRC, Cartilage growth and repair, Italy, June, 2005; ASBMR, September 2005, Nashville; MHE coalition meeting, November 2005, Houston; Craniofacial development, GRC, Ventura, January, 2006; FGF GRC, March 2006, Ventura; FASEB-Experimental Biology, San Francisco, April, 2006; Growth Plate Workshop, June 2006, Portland; Endocrine Society, June, 2006, Boston; Mouse Molecular Genetics, September, 2006; Esteve Symposium, October, 2006, Spain; American Academy Orthopaedic Surgery, October, 2006, Toronto; Spring Brain Conference, Sedona, AZ, March, 2007; Palmiter symposium-RP65, Seattle, April, 2007;

### **Future conferences**

Intracellular Transport and Signal Transduction in Cancer Biomedicine, Norway, May 2007  
 CSHL mouse course, June, 2007  
 FGF signaling Gordaon Conference, Italy, March 2008

### **Teaching**

Nucleic Acids, Discussion Section Leader, Fall 1993, Fall 1994  
 Molecular Cell Biology, Discussion Section Leader (10 hr), Fall 1995-1998  
 Advanced Genetics, Lecture, (2 hr) Spring 1995, (3 hr) Spring 1996-2007  
 Molecular Biology and Pharmacology Journal Club, organizer, 1993/1994  
 Molecular and Developmental Biology Journal Club, organizer, 1995-2000  
 Central questions in Cell Biology, Lecture (4 hr), Fall 1995  
 Molekoolz, the course, Lecture (1.5 hr), winter 1996, winter 1997, winter 2000.  
 Molecular Neurobiology, Lecture (1 hr), winter 1997  
 Bio5011, Ethics in Research Science, Section Leader, winter 1997  
 Signaling and Human Biology, Section organizer (8 hr), lecture (1 hr.) discussion (2 hr.), Spring 2002, 2003  
 Developmental Biology and Disease, Medical student elective, 3 hr, Spring 2006, 2007

### **Student Mentoring**

Current Ph.D. students in lab:

Sung-Ho Huh  
Euysoo Kim  
Monica Vega-Hernandez  
Marie Kozel

Past students in lab:

Huacheng Ying, MS, July 1996, Thesis title: Positional cloning of the tilted locus,  
Don McEwen, Ph.D., January, 1998, Thesis title: FGFR3 gene regulation, Current, Postdoctoral fellow with Mark Peifer, University of North Carolina, Assistant professor, University of Texas, Austin, 2006-  
Jennifer Colvin, M.D. Ph.D. March, 1999, Thesis title: Developmental role of FGFR3 and FGF9, MD, 2001, Current, Fellow in Child Psychiatry, Duke University Medical School.  
Jingsong Xu, Ph.D. September, 1999, Thesis title: Midbrain-hindbrain development, , Postdoctoral fellow with Steve Shapiro, Harvard Medical School, Current, Research Associate, Harvard Medical School.  
Qing Wang, Ph.D. February, 2001, Studies of mice lacking FGF14, Current position, patent division, Monsanto Inc, St. Louis, MO.  
Wenlin Yuan, Ph.D., June, 2002, biology of slit genes. Current, postdoctoral fellow with Timothy Ley, Washington University Medical School  
Kai Yu, Ph.D., July, 2002, FGF receptor 2 function in bone growth and development. Current, postdoctoral fellow in my laboratory.  
Zhonghao Liu, Ph.D. August, 2003, FGF18 signaling in bone growth and vasculogenesis. Current, postdoctoral fellow with Alan Permutt, Washington University Medical School.  
JL Lou, Ph.D. January, 2005, The Modulation of Voltage-Gated Sodium Channels and Neuronal Excitability by FGF14. Current, Resident in Internal Medicine, Duke University.  
Andrew White, Ph.D. March 2005, Fibroblast Growth Factor 9 Regulates Mesenchymal Gene Expression and Regional Proliferation to Coordinate Developing Lung Shape and Size with Epithelial Morphogenesis and Blood Vessel Vasculogenesis. Current, postdoctoral fellow, Ornitz lab  
Inna Hughes, Ph.D. mechanism of Otopetrin 1 regulation of cellular calcium. December, 2005, Current, MSTP student.  
Kory Lavine, Ph.D. May, 2006, Heart vascular development, MSTP student  
Chad Perlyn, M.D., Ph.D. (Oxford University Ph.D. June 2006), Fellow in plastic surgery, WUSM.

Current postdoctoral fellows:

Maolei Xiao, Ph.D.  
Kai Yu, Ph.D.  
Hidemi Kanazawa, M.D., Ph.D.  
Yongjun Yin, Ph.D.  
Andrew White, Ph.D.  
Fernanda Laezza, M.D, Ph.D.

Past postdoctoral fellows:

Becky Green, M.D., Ph.D. 1999-present instructor, Pediatric Endocrinology, St. Louis Children's Hospital  
Mike Naski, M.D., Ph.D. 1997-present, Assistant Professor, UT San Antonio  
Al Blunt, M.D. (Covance Inc.)



Yunxia Wang, Ph.D. 1998-present, Research Assistant Professor, U. Nebraska-Medical Center  
 Arasu Chellaiah, Ph.D. (self employed)  
 Sylvia Santos-Ocampo, M.D. 1995-present, Clinician  
 Luke Bruns, M.D. 1999-present, Clinician  
 Belen Hurle, Ph.D., 2002-present, Research Associate, NIH  
 Zhonghao Liu, Ph.D., 2004-present, postdoctoral fellow with Alan Permut  
 Irene Hung, M.D. 2002-2005, Genetics fellow, Department of Pediatrics., University of Utah  
 Anne Jacob, Ph.D. Research Associate, University of Oslo,  
 Xiuqin Zhang, Ph.D., Faculty, Beijing University.

### **Committees**

Molecular and Cellular Biology Steering Committee, 1992-present  
 Transgenic/Barrier Sub-Committee, 1995-present  
 Washington University Cancer Center, Basic Science Sub-Committee, 1995-present  
 Developmental Biology Steering Committee, 1997-present  
 Mouse behavior core steering committee, 1999-present  
 Member, Washington University Advisory Board to Sigma -Aldrich Research, Molecular Biology Product Initiatives, 1997 – 2001.  
 Member, Scientific Advisory Board, Sigma-Aldrich, 2002-present.  
 Committee for Research Integrity, Ad hoc member, May 2002. July 2005  
 Executive Faculty, Washington University 10/2004-present.

### **Directorships**

Washington University Cancer Center Developmental Biology group. June 1997-present  
 Program in Developmental Biology, Division of Biology and Biomedical Science. May 1998-May 2001.

### **Conference chair**

Gordon Research Conference on Fibroblast Growth Factors in Development and Disease. March, 2006.

### **Reviewing**

Cell; Nature; Genes & Development; Science; Neuron; Development; Nature Genetics; Nature Medicine; Developmental Biology; Developmental Dynamics; Mechanisms of Development; J. Biological Chemistry; Biochemistry; J. Cell Biology; J. Cell Physiology; Blood; Nucleic Acid Research; J. Neuroscience; J. Cellular Biochemistry; Transgenic Research; PNAS; Molec. Endocrinology; Exp. Eye Research; Cancer Communications; Endocrine Review; Oncogene; J. Bone Mineral Research; Bone; Human Molecular Genetics; J. Clinical Investigation; others

### **Study sections**

Ad hoc reviewer for NIH-CBY-1, October 1998  
 Ad hoc reviewer for NIH-CDF-5, June 1999  
 Beckman Young Investigator Program, November, 1999, November 2000, November 2001  
 Special emphasis panel for NIH HL-99-024, Genomic applications for Heart, Lung and Blood Research, June 2000  
 Special emphasis panel for NIH DC-01-00, Studies of sensory-motor functions responsive to gravity in genetically altered model systems, April, 2001.  
 Special emphasis panel for NIH DA-01-011, Insertional mutagenesis in the mouse, July, 2001  
 NIDCD Special emphasis panel for NIH PAR-01-103, November, 2001  
 NIDCD, ZDC1 SRB-A, ad hoc member, November, 2002

NCI, Cancer center site visit, Columbia University, January, 2003  
 Ad hoc reviewer, NIH-BIO, Biochemistry Study Section, March, 2003  
 Ad hoc reviewer, Pathobiochemistry study section, February, 2004  
 NCI, internal review, Fredrick MD, April, 2004  
 ZRG1 MDCN-A study section, July, 2004  
 ZRG1 CDD- Cardiovascular Differentiation and Development study section, October 2004  
 Dev2, member, 2005-2009

### **Societies**

American Association for the Advancement of Science (AAAS)  
 Society for Developmental Biology (SDB)  
 Society for Neuroscience (SfN)

### **Editorial board**

Developmental Dynamics

### **Research Abstract**

Fibroblast growth factors (FGFs) are essential molecules for mammalian development. Members of the FGF family regulate cell proliferation, migration and differentiation. Engineered mutations in the genes encoding several FGFs and FGF receptors (FGFRs) result in developmental defects and/or embryonic lethality. Additionally, gain of function point mutations in the genes encoding FGFRs 1, 2 and 3 results in hereditary craniofacial and skeletal dysplasias in humans.

We have recently discovered that a subfamily of FGFs (FHF4s) acts intracellularly in neurons and is important for neuronal signal transduction. Disruption of the intracellular signaling molecule, FGF14/FHF4 results in an anatomically normal mouse with severe neurobehavioral phenotypes including ataxia, paroxysmal dystonia and cognitive impairment. We are interested in the mechanism by which FGF14 regulates neuronal excitability in the cerebellum and hippocampus. We are also studying how FGF14/FHF4 regulates presynaptic function and short and long-term potentiation.

We are also studying the more classical FGFs and FGF receptors in mouse embryogenesis. Using knockout and conditional knockout technology we have constructed FGF and FGF receptor mutants with defects in skeletal, lung, heart and CNS development. These mutant mice are being studied as developmental model systems for branching morphogenesis, vasculogenesis and skeletal and neuroepithelial patterning and growth. These mice are also being used as material for microarray profiling studies to identify interacting gene families.

### **Future directions**

My laboratory will continue to study the function of FGF signaling in four main areas:

1. Central nervous system development and neurophysiology
2. Lung development
3. Heart development
4. Skeletal development

Goals will be to identify novel interacting signaling molecules and novel downstream effectors of FGF signaling. In addition to focusing on existing FGF ligand knockout mice we have now made a functional conditional allele for FGF receptor 2. We will inactivate FGF receptor 2 using tissue-specific and temporal-specific expression of Cre recombinase. Novel techniques that are being applied include microarray analysis of knockout mice, organ culture and bead implantation on tissue derived from knockout mice.

We will continue to work on understanding the molecular and developmental function of the *Otopetrin* gene. A mutation in *Otopetrin* is responsible for the tilted mouse phenotype.

*Otopetrin* was positionally cloned in my laboratory. Collaborative experiments are planned to examine Otopetrin expression and function in the vestibular system at different gravitational intensities.